Amendment to the Claims

The following listing of claims replaces all prior versions of the claims pending in this application. Please cancel claims 2-16 without prejudice to their subsequent introduction into this application or a related application.

1. (Original) A GHRH analogue, a functional derivative of said analogue, or a pharmaceutically acceptable salt thereof comprising formula X: Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-A9-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-A21-A22-Leu- Gln - Asp - Ile- Met - Ser -Arg-A30- NH_2, wherein

   A2 is Ala or D-Ala;

   A8 is Asn, D-Asn or Ala;

   A9 is Ser or Ala;

   A10 is Tyr or D-Tyr;

   A15 is Gly, Ala or D-Ala;

   A21 is Lys or D-Lys;

   A22 is Leu, D-Leu, Lys or Ala; and

   A30 is a bond or any amino acid sequence of 1 up to 15 residues;

   said analogue, functional derivative of said analogue or salt thereof having an *in vitro* potency index substantially higher than the *in vitro* potency index of a naturally occurring GHRH.

2. – 16. (Canceled)

17. (Previously Presented) A GHRH analogue or a pharmaceutically acceptable salt thereof able to stimulate secretion or synthesis of growth hormone in a mammal, said GHRH analog or pharmaceutically acceptable salt having an *in vitro* potency index substantially higher than the *in vitro* potency index of a native hGHRH1-29 and having formula Tyr- D-Ala^{2}-Asp-Ala-Ile-Phe-Thr-Asn- Ser-D-Tyr^{10}-Arg-Lys-Val-Leu- D-Ala^{15}-Gln-Leu-Ser-Ala-Arg-Lys-Lys^{22}-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein A30 is a bond or any amino acid sequence of 1 up to 15 residues.

18. (Previously Presented) A GHRH analogue according to claim 17, wherein the *in vitro* potency index is at least 500-fold higher than the *in vitro* potency index of a native hGHRH1-29.

19. (Previously Presented) The GHRH analogue of claim 18, wherein the *in vitro* potency index is at least 1500-fold higher than the *in vitro* potency index of a native hGHRH1-29.

20. (Previously Presented) The GHRH analogue of claim 19, wherein the *in vitro* potency index is at least 2500-fold higher than the *in vitro* potency index of a native hGHRH1-29.

21. (Previously Presented) The GHRH analogue of claim 17, wherein said GHRH analogue has the formula Tyr- D-Ala^{2}-Asp-Ala-Ile-Phe-Thr-Asn- Ser-D-Tyr^{10}-Arg-Lys-Val-Leu- D-Ala^{15}-Gln-Leu-Ser-Ala-Arg-Lys-Lys^{22}-Leu-Gln-Asp-Ile-Met-Ser-Arg -NH_2.

22. (Previously Presented) A pharmaceutical composition, comprising:

a) an effective amount of a GHRH analogue or a pharmaceutically acceptable salt thereof comprising formula X:Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-Lys-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein
A2 is Ala or D-Ala;
A8 is Asn, D-Asn or Ala;
A10 is Tyr or D-Tyr;
A15 is Gly, Ala or D-Ala;

A22 is Leu, D-Leu, Lys or Ala; and

A30 is a bond or any amino acid sequence of 1 up to 15 residues and wherein said analogue comprises at least one amino acid substitution in the native form of hGHRH1-29; and;

b) a pharmaceutically acceptable carrier.

23. (Previously Presented) The pharmaceutical composition of claim 22, wherein said GHRH analogue or salt thereof is selected from the group consisting of, and wherein:

- A2 is D-Ala, A8 is Ala, A15 is Ala, A22 is Lys;
- A2 is D-Ala, A10 is D-Tyr, and A22 is Lys and;
-A2 is D-Ala, A10 is D-Tyr, A15 is D-Ala, and A22 is Lys.

24. (Previously Presented) The pharmaceutical composition of claim 23, wherein A2 is D-Ala, A8 is Asn, A10 is D-Tyr, A15 is D-Ala, A22 is Lys and A30 is a bond.

25. (Previously Presented) A pharmaceutical composition, comprising:

a) an effective amount of a GHRH analogue or a pharmaceutically acceptable salt thereof of formula X:Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-Lys-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein

A2 is Ala or D-Ala;

A8 is Asn, D-Asn or Ala;

A10 is Tyr or D-Tyr;

A15 is Gly, Ala or D-Ala;

A22 is Leu, D-Leu, Lys or Ala; and

A30 is a bond or any amino acid sequence of 1 up to 15 residues and wherein said analogue comprises at least one amino acid substitution in the native form of hGHRH1-29; and;

b) a pharmaceutically acceptable carrier.

26. (Previously Presented) The pharmaceutical composition of claim 25, wherein said GHRH analogue or salt thereof is selected from the group consisting of, and wherein:

- A2 is D-Ala, A8 is Ala, A15 is Ala, A22 is Lys;
- A2 is D-Ala, A10 is D-Tyr, and A22 is Lys and;
-A2 is D-Ala, A10 is D-Tyr, A15 is D-Ala, and A22 is Lys.

27. (Previously Presented) The pharmaceutical composition of claim 26, wherein A2 is D-Ala, A8 is Asn, A10 is D-Tyr, A15 is D-Ala, A22 is Lys and A30 is a bond.

28. (Previously Presented) A pharmaceutical composition for stimulating secretion or synthesis of growth hormone in a mammal in need thereof, the pharmaceutical composition comprising:

a) an effective amount of a GHRH analogue or a pharmaceutically acceptable salt thereof comprising formula X:Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-Lys-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2 , wherein
A2 is Ala or D-Ala;
A8 is Asn, D-Asn or Ala;
A10 is Tyr or D-Tyr;
A15 is Gly, Ala or D-Ala;
A22 is Leu, D-Leu, Lys or Ala; and
A30 is a bond or any amino acid sequence of 1 up to 15 residues and wherein said analogue comprises at least one amino acid substitution in the native form of hGHRH1-29, and;

b) a pharmaceutically acceptable carrier.

29. (Previously Presented) The pharmaceutical composition of claim 28, wherein said GHRH analogue or salt thereof is selected from the group consisting of, and wherein:

- A2 is D-Ala, A8 is Ala, A15 is Ala, A22 is Lys;
- A2 is D-Ala, A10 is D-Tyr, and A22 is Lys and;
-A2 is D-Ala, A10 is D-Tyr, A15 is D-Ala, and A22 is Lys.

30. (Previously Presented) The pharmaceutical composition of claim 29, wherein A2 is D-Ala, A8 is Asn, A10 is D-Tyr, A15 is D-Ala, A22 is Lys and A30 is a bond.

31. (Previously Presented) The use of a GHRH analogue, or a pharmaceutically acceptable salt thereof in the preparation of a pharmaceutical composition for stimulating secretion or synthesis of growth hormone in a mammal in need thereof, said GHRH analog or pharmaceutically acceptable salt comprising formula X: Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-Lys-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein

A2 is Ala or D-Ala;

A8 is Asn, D-Asn or Ala;

A10 is Tyr or D-Tyr;

A15 is Gly, Ala or D-Ala;

A22 is Leu, D-Leu, Lys or Ala; and

A30 is a bond or any amino acid sequence of 1 up to 15 residues and wherein said analogue comprises at least one amino acid substitution in the native form of hGHRH1-29.

32. (Previously Presented) The use as defined in claim 31, wherein said GHRH analogue or salt thereof is selected from the group consisting of, and wherein:

- A2 is D-Ala, A8 is Ala, A15 is Ala, A22 is Lys;
- A2 is D-Ala, A10 is D-Tyr, and A22 is Lys and;
-A2 is D-Ala, A10 is D-Tyr, A15 is D-Ala, and A22 is Lys.

33. (Previously Presented) The use as defined in claim 32, wherein A2 is D-Ala, A8 is Asn, A10 is D-Tyr, A15 is D-Ala, A22 is Lys and A30 is a bond.

34. (Previously Presented) The use according to claim 31, wherein said mammal has a disorder selected from the group consisting of hypothalamic pituitary dwarfism, burns, osteoporosis, renal failure, non-union bone-fracture, acute/chronic debilitating illness or infection, wound healing, reduction of the incidence of post-surgical problems, lactation failure, infertility in women,

cachexia in cancer patients, anabolic and/or catabolic problems, T-cell immunodeficiencies, neurodegenerative conditions, GHRH receptor-dependent tumors, aging, sleep disorders, muscle wasting diseases such as-in sarcopenic patients, frail elderlies, HIV patients and cancer patients having radiotherapy and chemotherapy side-effects.

35. (Previously Presented) The use according to claim 34, wherein said muscle wasting diseases are selected from the group consisting of; sarcopenia, frailty in elderlies, HIV and cancer.

36. (Previously Presented) The use of a GHRH analogue, or a pharmaceutically acceptable salt thereof for stimulating secretion or synthesis of growth hormone in a mammal in need thereof, said GHRH analog or pharmaceutically acceptable salt comprising formula X: Tyr-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-A10-Arg-Lys-Val-Leu-A15-Gln-Leu-Ser-Ala-Arg-Lys-A22-Leu-Gln-Asp-Ile-Met-Ser-Arg-A30-NH_2, wherein

A2 is Ala or D-Ala;

A8 is Asn, D-Asn or Ala;

A10 is Tyr or D-Tyr;

A15 is Gly, Ala or D-Ala;

A22 is Leu, D-Leu, Lys or Ala; and

A30 is a bond or any amino acid sequence of 1 up to 15 residues and wherein said analogue comprises at least one amino acid substitution in the native form of hGHRH1-29.

37. (Previously Presented) The use according to claim 36, wherein said mammal has a disorder selected from the group consisting of hypothalamic pituitary dwarfism, burns, osteoporosis, renal failure, non-union bone-fracture, acute/chronic debilitating illness or infection, wound healing, reduction of the incidence of post-surgical problems, lactation failure, infertility in women, cachexia in cancer patients, anabolic and/or catabolic problems, T-cell immunodeficiencies, neurodegenerative conditions, GHRH receptor-dependent tumors, aging, sleep disorders, muscle wasting diseases such as-in-sarcopenic patients, frail elderlies, HIV patients and cancer patients having radiotherapy and chemotherapy side-effects.

38. (Previously Presented) The use according to claim 37, wherein said muscle wasting diseases are selected from the group consisting of; sarcopenia, frailty in elderlies, HIV and cancer.